the general surgical case than it is for the posttonsillectomy patient." Perhaps the more exact and definite knowledge which is available concerning the immediate course following the general surgical operation is responsible for the present feeling that the abscesses following these operations are embolic in origin. The experimental evidence available, showing that intrapulmonary abscesses can be readily produced by the introduction of septic emboli into the blood stream, suggests that the postoperative abscesses seen clinically are largely due to infected emboli from the operative field.

I congratulate the author upon placing so large a series of pulmonary abscesses on record for statistical study and interpretation.

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HAROLD BRUNN, M. D. (384 Post Street, San Francisco)—The route of infection in abscesses of the lung is one that is still under very much discussion. It can of course be approached both from the clinical side and the experimental side. It is always very difficult, when looking over a long series of cases of hospital records with which one has had no intimate contact, to form definite judgments as to causations. Unless at the time of taking the history, one is particularly interested in bringing out the facts, we have found that in those cases with which we are conversant, they are frequently woefully lacking in a true statement of the actual state of affairs.

Recent experiments on animals have shown the possibility of creating lung abscesses both by the embolic and by the aspiration route. Both modes of infection are possible, and it is difficult clinically always to state the route of infection. One is inclined to believe, however, that those cases that take a poor anesthetic, with much mucus and coughing, and within twenty-four hours develop symptoms of an abscess, that such cases are aspiratory rather than embolic in origin. In many of the cases which we have had following tonsillectomies, such a history with a rapid onset of symptoms, has led us to believe that aspiration was the cause. In other cases with a late onset—after a week—it is more probable that the embolic theory would best explain the origin of the lung abscess.

The lesson to be learned is—first—that in order to avoid emboli, wounds should be carefully handled with as little retraction as possible, and—secondly—that a quiet anesthetic not too deep so that the cough reflex may come back early, with proper hygiene of the mouth such as using Berwick's dye as a preliminary, would tend to diminish also the aspiration route of lung abscesses.

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WILLIAM J. KERR, M. D. (University of California Medical School, San Francisco)—The author is to be congratulated upon his report of postoperative lung abscess cases. Statistical studies in this direction have been meager because many patients who develop pulmonary complications after tonsillectomy have their symptoms after leaving the hospital. In many instances they probably report to other physicians or go to other hospitals for subsequent treatment.

The incidence of pulmonary complications after other operations which require longer hospitalization during convalescence are more generally recognized and studied. I think that one who has followed the literature of postoperative lung abscess, or other pulmonary complications, is impressed with the divergent opinions as to the cause of the involvement of the lung. There cannot be much doubt, I think, that where lung abscess or other pulmonary complications arise, following operation under local anesthesia in different parts of the body, that the process is more likely to be an embolic one.

However, lung abscess that occurs following tonsillectomy or other operations on the throat or pharynx may have two routes of infection. I think that the work of Lemon and his associates indicates the possibility, in fact the strong probability, that operation on the tonsils will lead to pulmonary infection. The abolition of the cough reflex during anesthesia here plays apparently a very important rôle in the spread of the infection along with the inhalation of infected material.

The statistical studies that have been reported from different parts of the country indicate that in those centers where tonsils are done with the patient in a sitting posture, or without proper local drainage, there is greater incidence of pulmonary complications than where suction is used at the time of operation, or where the patient's head and shoulders are kept in a lower position. One cannot escape the suggestion that has been made by some that infected thrombi in the peritonsillar vessels may break off and be carried to the right heart, thence to the lung, or that infection may spread by way of lymphatics to the pulmonary tissues.

The diagnosis of lung abscess, whether it follows a tonsillectomy or any other operative procedure, or whether it follows some other infection in the lung, has at times been somewhat difficult to make. The x-ray, of course, is of tremendous value in locating the abscess in the deeper tissues. We have not been particularly impressed by the use of the injection of opaque oils, such as lipiodol, because of the difficulty of getting this material in the abscess cavity. Bronchoscopy, with injection of the opaque oil at the same time where the injection could be properly directed, may at times show the limitations of the cavity or cavities.

In the treatment of lung abscess we must keep in mind the fact that a fairly high percentage of the cases will recover without surgical intervention. Rest, diet, inhalations of various type with postural drainage may be all that is necessary to bring about a cure. However, if the cavities do not empty freely, we have found it of value to do a bronchoscopy which may help to open up the channels to the bronchi or, by washing out the cavity, we may assist in the drainage. If the abscess is close to the chest wall and does not heal by the expectant method, surgery should be given consideration. If the lung is not adherent to the chest wall, pneumothorax may be of great advantage in helping to clear up the process. The most difficult problem that we have in the treatment of lung abscess is seen in the patient who has gone on for weeks or months, who is more or less stationary with mild attacks of fever and general symptoms of abscess cavity, showing a fairly thick fibrotic wall. It is in this group of cases that medical treatment will probably be of little value. Artificial pneumothorax may even in these be of some help, but more likely will require surgery, either with drainage or with drainage and cautery.

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## ARSENICAL OPTICAL NEURITIS—WITH SPECIAL REFERENCE TO SYPHILIS*

### CASE REPORTS

*By* GEORGE NEWTON HOSFORD, M. D.
*San Francisco*

DISCUSSION *by Lloyd Mills, M. D., Los Angeles; Milton B. Lennon, M. D., San Francisco; Lovell Langstroth, M. D., San Francisco.*

THIS subject was brought to my attention in January, 1926, by the following cases:

A man of 25, whom I had refracted two months before, came to me with a history of blurring of vision, which had begun rather suddenly. I had noted, when I first examined him, an extensive disseminated choroiditis which had involved the right macular region and had missed the left macular region by a fraction of a millimeter. His vision with his correction was 0.2 in the right

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eye, and normal in the left. The disease process was obviously of long standing. The patient was an ignorant workman and would not undergo the extensive examination which is often necessary to determine the cause of such a condition. I felt that the damage had been done, so merely refracted him. When he returned I expected to find an exacerbation of his choroiditis, but instead he had numerous very minute deposits on Descemet's membrane in both eyes, and his optic nerves and the adjacent retina were edematous and slightly hyperemic.

In the two-month interval, between the time when I refracted him and his second visit, he had acquired a chancre. He had gone immediately to a doctor, and the doctor had instituted treatment. When I saw him with his optic neuritis he had received four doses of neosalvarsan and was having daily mercurial inunctions.

Now the question arose, "Was the neuritis due to the syphilis or to the neosalvarsan?"

### VIEWPOINTS IN THE LITERATURE

The standard textbooks of ophthalmology state that it is due to the liberation of luetic toxins. The treatment advised is to continue the use of the drug, or even to increase the dose. I discussed the matter with a neurologist and he was of the same opinion and cited cases of his own where he had obtained an increased cell count in the cerebrospinal fluid in comparable cases. This, he interpreted as a reaction to the invasion of the central nervous system by the *Spirochaeta pallida* even at that early stage of the disease.

On the other hand, we know that among the untoward actions of arsenicals is irritation of nervous tissue.

### OPTIC NEURITIS FOLLOWING SALVARSAN THERAPY

The ocular manifestations of syphilis have interested all practicing physicians for years, and in going through the literature we find, in the reports of societies, whole sessions devoted to the discussions of ocular lues. These reports begin to have a particular interest for us about the year 1910, when salvarsan was introduced by Ehrlich.

The eye section of the British Medical Association devoted a session of its 1912 meeting to the consideration of lues of the eye and its treatment by salvarsan. There were a number of carefully prepared papers on various phases of the subject, and much earnest discussion.

Doctor Walker of Liverpool had seen several cases of optic neuritis following the administration of salvarsan and admitted frankly that he did not know whether the neuritis was due to the disease or the drug. He cautioned his colleagues not to forget general principles and to remember their experiences with atoxyl. Blindness from atoxyl was not reported until two years after the introduction of the drug and then, within a few months, over two hundred cases were reported in the literature by different workers.

In 1913 the St. Louis Medical Society held a symposium on ocular syphilis. One paper by William F. Hardy reports two cases and refers to a third treated by another oculist. In the first case a very violent bilateral neuroretinitis occurred four weeks after an injection of salvarsan. The neuroretinitis was attributed to the lues and another salvarsan given. The disease progressed from bad to worse, and the patient became blind. A second case received one injection. Three months later the patient developed a neuroretinitis and iridocyclitis. Inunctions and local treatment were ordered and the condition improved under these measures. The result, however, was practical blindness, as it was also in a third case.

He admits, as anyone would, that the salvarsan may have had nothing to do with these unfortunate results, particularly in the second and third cases. Such things may happen under mercury alone. A hitherto well eye may become inflamed, while a similar process is subsiding in the other eye, with the patient thoroughly mercurialized at the time.

On the other hand, in the same meeting we have John Green, quoting a German report, where 63 per cent of seventy-six cases of neuroretinitis had a rapid and satisfactory result. Ehrlich himself, however, warned against the use of salvarsan in any patient who showed signs of optic neuritis, and it was some time before the ophthalmologists ventured to use it in such cases. Green concludes that when such lesions are certainly luetic salvarsan is indicated, although the best results are obtained when the drug is combined with mercury and iodides.

The report of the discussion of the treatment of syphilitic eye lesions by the Ophthalmological Society of the United Kingdom occupies fifty pages of their transactions in the year 1916.

On the question of salvarsan and optic neuritis J. B. Lawford quotes from a monograph by Dor the following evidence: "In records published from 1850 to 1911 he found five cases of severe papillitis and gumma of the optic papilla; between 1911 and 1914 he found ten." Wernicke gives the following facts: "In 1912 a death occurred in Odessa, following the administration of salvarsan. This led to a temporary abandonment of the drug by the medical men of the town. They reverted to mercurial treatment alone. During the twelve months, in 1911 and 1912, while salvarsan was in use, he had referred to him ten cases of acute optic neuritis in syphilitics treated with the drug. In the subsequent twelve months, while the drug was not in use, not a single case came under his observation.

In 1923 we find the pendulum swinging the other way. In this year a paper on the treatment of ocular syphilis was read by E. A. Shumway to the College of Physicians of Philadelphia. In this paper he devotes a paragraph to the conditions we have been considering. He says: "In luetic optic neuritis mercury has always been successfully employed. When salvarsan was introduced many cases of optic neuritis were discovered, and it was assumed that they were due to an arsenical intoxication, which had undoubtedly been the case with previous use of atoxyl. Many

controversies as to the true nature of these so-called neurorecidives were carried on and progress in the treatment of syphilis of the central nervous system was greatly retarded because of the fear of their appearance. Syphilologists found, however, on more careful examination of their cases before treatment that the frequency of such lesions was nearly as great as those reported due to salvarsan, and fortunately it was found that additional large doses of salvarsan, administered after the development of the nerve lesions, had a tendency to cause a disappearance of the symptoms, and nearly all ophthalmologists follow the advice of syphilologists in advocating the use of combined treatment with salvarsan injections and mercury, obtaining in this way as intensive a therapy as possible, in order to avoid the blindness which must result from long-continued inflammation."

As he unfortunately speaks in generalities, and does not give case records and statistics, one is inclined to be skeptical as to the value of this opinion.

A particularly able discussion of the ocular effects of tryparsamid by Cady and Alvis of St. Louis appeared in the *Journal of the American Medical Association* of January 6, 1926. The literature of the subject is reviewed and is inclusive just as in the condition we have discussed. Their own series consisted of 153 patients who were considered normal. That is, they had no recognizable signs of neuritis, atrophy or diminution in visual acuity or perimetric fields. There were also twenty-seven cases considered abnormal because of the presence of one or more of the foregoing signs or symptoms.

Of the 153 normal patients eight, or 5.2 per cent, had sufficient manifestations to warrant their tabulation. Among this eight, three had slight contraction of the fields which disappeared after temporary withdrawal of the drug, and of five with marked constriction two failed to improve. So that 1.3 per cent of normal patients were injured by the use of tryparsamid.

Of the twenty-seven abnormal patients ten, or 37 per cent, became worse. Six of the ten had recognizable atrophy at the start, while four had slightly, or moderately, constricted fields at the start. Four, or 14 per cent, of the twenty-seven were noticeably improved, while thirteen, or 48.2 per cent, remained the same. Three of the patients with optic atrophy progressed to blindness. The patients who suffered permanent injury were treated early in their experience with the drug.

### EXPERIMENTAL STUDIES

So much for clinical reports. Now let us turn to the experimental phase of the question:

In 1924 an article by Young and Loevenhart of the University of Wisconsin on "The Relation of the Chemical Constitution of Certain Organic Arsenical Compounds to Their Action on the Visual Tracts" appeared in the *Journal of Pharmacology and Experimental Therapeutics*. It is a masterly investigation into an exceedingly complex subject. They investigated merely the power of these compounds to produce changes in the optic tracts, and not the nature or mechanism by which such changes were produced. Their method was first to determine the minimal lethal dose for rabbits for each compound. They then took a group of animals, from three to twenty-three in number, upon which to try each compound, and injected them intravenously at weekly intervals with a dose that averaged about 25 per cent of the minimal lethal dose. For example, they took twenty rabbits and gave them tryparsamid. The M. L. D. was found to be 1.25 grams per kilo. Twenty-five per cent of this was computed for each rabbit, and given in an ear vein once a week. At the same time the rabbits were examined with the ophthalmoscope. The number of doses given varied considerably, but if lesions were not produced sooner they were given eight to twelve doses. At the end of the experiment the animals were killed by air embolism and the eyes taken for microscopic study. The eyes of six normal rabbits were studied as controls.

The nineteen compounds studied were divided into five groups on the basis of their structure. First they studied representative inorganic arsenicals; next, organic arsenicals without an amino group; and finally, arsenicals with the amino group in the ortho, meta, and para position, with reference to the arsenic.

In four of these classes the arsenic may be either trivalent or pentavalent. At least one trivalent and one or more pentavalent compounds were used in each group. Three arsenical compounds are known to produce visual tract lesions: *viz.*, atoxyl arsacetin, and tryparsamid.

The three have certain characteristics in common: (1) The arsenic is pentavalent. (2) They all have an amino, or substituted amino group, occupying the position para to the arsenic.

All of these substances produced lesions in rabbits, as did also several others of the same general structure. The ophthalmoscopic appearance usually began to change after the third or fourth dose. The optic cup would become filled, the nerve head blurred, and in the more marked cases there were hemorrhages in the retina and the vitreous became cloudy.

Arsphenamin and neoarsphenamin in which the amino group, or substituted amino group, is in the meta position were tried out on only three rabbits each, but the experiments ran for thirteen weeks with the arsphenamin, and nine with the neoarsphenamin. No lesions were produced. There is a footnote on neoarsphenamin stating that the minimal lethal dose varied from 150 to 275 milligrams per kilo, depending on the drug and the company that made the drug. This may be a clue as to why some patients develop optic-tract lesions from neosalvarsan, and why the great majority do not. Of course these experiments do not accurately reproduce the condition that we face in the human subject. The rabbits were not diseased, and the susceptibility of the human optic tract may differ from that of the rabbit to the same arsenical compound. The experimenters quoted were aware of this and, in fact, called

attention to it. The dosage used in the experiments were also greater than would be administered to human beings.

It may be false logic to withhold arsenicals in cases of syphilis showing optic-tract lesions, and time may show that these are the very cases where such therapy is most valuable, but in the present state of our knowledge of the subject it seems wise to proceed with caution in these cases.

In the patient who was under my observation, improvement in the optic neuritis was observed within two weeks after the neoarsphenamin was discontinued. Within six weeks all signs of the inflammation had disappeared. His antiluetic treatment was continued with mercury and bismuth, and I feel that our course in stopping the arsenical was probably correct.

490 Post Street.

DISCUSSION

LLOYD MILLS, M. D. (609 South Grand Avenue, Los Angeles)—Several years ago a physician came to me with a story of a minor incision of a finger occurring during an operation on a syphilitic patient. He gave this wound immediate attention, no local lesion developed, and repeated Wassermanns were negative. In spite of this he developed a definite and increasing syphilophobia. To allay his fears he went to a number of physicians and pleaded for a protective course of salvarsan from each on preventive grounds, stressing his psychic need.

I saw him after about two years of treatment and found a definite hemorrhagic neuroretinitis. The inevitable outcome was explained to him and every attempt made to deter him from further treatment, but he persisted and when last seen was blind from total arsenical atrophy of both optic nerves and central retinal degeneration.

A second case of cured syphilis, with negative Wassermanns for several years, was treated with neoarsphenamin every three months. Each injection was followed, in the eye having a posterior polar cataract, by a definite inflammation of the optic nerve which gradually began to whiten. These treatments were concealed until the man was obliged to disclose his history or go elsewhere. Improvement in the ocular condition followed and has been maintained since discontinuing these needless injections.

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MILTON B. LENNON, M. D. (380 Post Street, San Francisco)—Doctor Hosford's paper calls attention to a question that was first mooted shortly after Ehrlich had introduced salvarsan, a question that has not been fully answered even today.

That an optic neuritis can and does occur in the early stages of syphilis is indisputable—that it is a frequent accompaniment of late syphilis, particularly of the cerebral forms, has long since been recognized. Salvarsan and its various offsprings have increased the incidence of optic neuritis by a small percentage. This may be due either to its direct influence or by its freeing neurotoxins. The Herzheimer reaction is well recognized and is usually the result of using a small, almost tentative dose of salvarsan. A second generous dose will, as a rule, clear up the situation. Since this reaction is usually noted in patients beyond the early days of syphilis, it can be avoided by giving a preliminary course with mercury and iodides, and in generous doses. These invaluable remedies have been pushed too much aside since the introduction of salvarsan, and by many their true and extraordinary values are hardly recognized. They may not attack the spirochaetes with the valor of the salvarsan, but they can break down the products of syphilis whether these be arteritic, meningitic, or gummatous, in a way that salvarsan is in no way calculated to do.

We have little to fear in the way of an optic neuritis from salvarsan as is evidenced by few ill consequences from its use amid its universal employment. Even in ill-advised overdoses sufficient to produce a polyneuritis that lasted for months there were no residual effects to the optic nerve. It is well to ask ourselves, in any given syphilitic patient with optic neuritis, if salvarsan is playing a part. A disturbed kidney function may be the cause. With an upset gastro-intestinal system I have seen an optic neuritis in a syphilitic cleared up by mild saline cathartics; hence we should not blame salvarsan for an optic neuritis until we are sure that nothing in our way of investigation or treatment is not primarily at fault.

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LOVELL LANGSTROTH, M. D. (490 Post Street, San Francisco)—The fundamental problem behind this question is just why a small percentage of patients treated with salvarsan preparations develops optic neuritis. Syphilitic infection may bear no relation to it at all. In fact, since the great proportion of syphilitics escape it seems possible that it is not a question of liberation of syphilitic toxins at all but entirely a reaction between this drug and certain susceptible persons. We have no accurate knowledge of the tissue qualities which make for this susceptibility, but from the frequency with which we find degenerative processes in the cardiovascular, locomotor and nervous systems of supposedly normal persons we may presume that degeneration is half the story. Persons with degenerative changes or with lowered resistance to infection stand strain very badly. In the case of Doctor Hosford's patient the marked choroiditis which antedated the syphilitic infection was perhaps a sign that this particular individual would not tolerate salvarsan.

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## THE LURE OF MEDICAL HISTORY

### AMBROISE PARÉ

*By* JEAN OLIVER, M. D.
*San Francisco*

A PLUTARCH of the sixteenth century, writing of the great who had preceded him, would have chosen without doubt among his subjects two names that stand out in the history of science, Andre Vesalius and Ambroise Paré. For you remember, Plutarch, after describing the lives of his heroes, groups them in pairs and adds his "comparison," setting forth their similarities and differences and detailing in orderly fashion the first, second, and third "advantage" of one over the other.

In political affairs the opportunities for such estimates are perhaps easily found—kings, emperors, and statesmen present themselves automatically and their lives and deeds are public matters to be weighed and judged. It is otherwise in the history of science. But if ever the method were applicable to the subject of our interest, it is in the case of the two whom we have mentioned. So let us see what it will bring forth.

They were born to the same times—Paré three years the elder. But to what different conditions: Vesalius into a noble family, the aristocracy of medicine and the university—the great grandfather, physician to the Emperor and rector of the University of Louvain; the grandfather, a physician and author of mathematical treatises; the father, personal physician and pharmacist to the Princess—Governess of the Low Countries—